

Listing of Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

What is claimed is:

- 1 Claim 1. (Currently amended) A partially thio-modified aptamer that binds to a
2 TGF-beta protein, wherein the partially thio-modified aptamer comprises one or more
3 thio-modifications on the aptamer backbone.
- 1 Claim 2. (Original) The aptamer of claim 1, wherein the TGF-beta protein
2 comprises a human TGF-beta.
- 1 Claim 3. (Original) The aptamer of claim 1, wherein the TGF-beta protein
2 comprises a TGF-beta dimer.
- 1 Claim 4. (Original) The aptamer of claim 3, wherein the TGF-beta dimer is a
2 homodimer.
- 1 Claim 5. (Original) The aptamer of claim 4, wherein the TGF-beta homodimer is a
2 TGF-beta 1, 2 or 3 homodimer.
- 1 Claim 6. (Original) The aptamer of claim 3, wherein the TGF-beta dimer is a
2 TGFbeta 1, 2 or 3 heterodimer.
- 1 Claim 7. (Previously presented) The aptamer of claim 1, wherein the aptamer
2 comprises the sequence and modifications of SEQ ID NO: 62.
- 1 Claim 8. (Original) The aptamer of claim 1, wherein the aptamer is achiral.
- 1 Claim 9. (Original) The aptamer of claim 1, wherein the aptamer further comprises
2 a detectable label.
- 1 Claim 10. (Original) The aptamer of claim 1, further comprising one or more
2 pharmaceutically acceptable salts.

- 1 Claim 11. (Original) The aptamer of claim 1, further comprising a diluent.
- 1 Claim 12. (Withdrawn) A partially thio-modified aptamer that binds to a TGF-beta
2 receptor.
- 1 Claim 13. (Withdrawn) The aptamer of claim 12, wherein the TGF-beta receptor is a
2 signaling receptor.
- 1 Claim 14. (Withdrawn) The aptamer of claim 12, wherein the TGF-beta receptor is a
2 co-receptor.
- 1 Claim 15. (Withdrawn) The aptamer of claim 13, wherein the TGF-beta signaling
2 receptor comprises a human TGF-beta signaling receptor.
- 1 Claim 16. (Withdrawn) The aptamer of claim 13 wherein the TGF-beta signaling
2 receptor comprises a TbetaRI or a TbetaRII receptor.
- 1 Claim 17. (Withdrawn) The aptamer of claim 13, wherein the target of the aptamer is
2 the GS domain of a TbetaRI receptor.
- 1 Claim 18. (Withdrawn) The aptamer of claim 14, where the co-receptor is TGF-beta
2 3.
- 1 Claim 19. (Withdrawn) The aptamer of claim 12, wherein the aptamer is achiral.
- 1 Claim 20. (Withdrawn) A partially thio-modified aptamer that binds to a ligand-
2 receptor complex comprising a TGF-beta ligand and a receptor complex comprising a
3 TbetaRI and a TbetaRII receptors.
- 1 Claim 21. (Withdrawn) The aptamer of claim 20, wherein the target of the aptamer is
2 the GS domain of a TbetaRI receptor.
- 1 Claim 22. (Withdrawn) The aptamer of claim 20, wherein the aptamer is achiral.

- 1 Claim 23. (Withdrawn) A partially thio-modified aptamer that binds to a ligand
2 binding trap capable of trapping TGF-beta ligands.
- 1 Claim 24. (Withdrawn) The aptamer of claim 23, wherein the ligand binding trap
2 comprises decorin, latency-associated protein (LAP) or alpha-macroglobulin.
- 1 Claim 25. (Withdrawn) The aptamer of claim 23, wherein the aptamer is achiral.
- 1 Claim 26. (Withdrawn) A partially thio-modified aptamer that binds to an auxiliary
2 protein that promotes binding of TGF-beta ligand to Tbeta signaling receptors.
- 1 Claim 27. (Withdrawn) The aptamer of claim 26, wherein the auxiliary protein is a
2 SARA protein.
- 1 Claim 28. (Withdrawn) The aptamer of claim 26, wherein the aptamer is achiral.
- 1 Claim 29. (Withdrawn) A partially thio-modified aptamer that binds to a Smad
2 protein.
- 1 Claim 30. (Withdrawn) The aptamer of claim 29, wherein the Smad protein is an R-
2 Smad, a Co-Smad, an I-Smad or a combination thereof.
- 1 Claim 31. (Withdrawn) The aptamer of claim 29, wherein the aptamer is achiral.
- 1 Claim 32. (Withdrawn) A partially thio-modified aptamer that binds to a TGF-beta
2 protein complex and enhances TGF-beta activity.
- 1 Claim 33. (Withdrawn) The aptamer of claim 32, wherein the binding site of the
2 aptamer on the TGF-beta protein complex comprises a region of a ligand binding trap
3 protein.
- 1 Claim 34. (Withdrawn) The aptamer of claim 32, wherein the binding site of the
2 aptamer on the TGF-beta protein complex comprises a region of an inhibitory I-Smad.
- 1 Claim 35. (Withdrawn) The aptamer of claim 32, wherein the aptamer is achiral.

- 1 Claim 36. (Withdrawn) A partially thio-modified aptamer that binds to a TGF-beta
2 protein complex and inhibits TGF-beta activity.
- 1 Claim 37. (Withdrawn) The aptamer of claim 36, wherein the binding site of the
2 aptamer on the TGF-beta protein complex comprises a region of an R-Smad or a Co-
3 Smad.
- 1 Claim 38. (Withdrawn) The aptamer of claim 36, wherein the aptamer is achiral.
- 1 Claim 39. (Withdrawn) A partially modified thioaptamer that inhibits TGF-beta
2 activity by binding to a TGF-beta ligand, a TGF-beta ligand-Tbeta receptor complex, a
3 TGF-beta signaling receptor and co-receptor, to an R-Smad or a Co-Smad.
- 1 Claim 40. (Withdrawn) The aptamer of claim 39, wherein the aptamer is achiral.
- 1 Claim 41. (Withdrawn) A partially modified thioaptamer that modifies TGF-beta
2 activity by binding to a TGF-beta ligand, a TGF-beta ligand-Tbeta receptor complex, a
3 TGF-beta signaling receptor and co-receptor, to an R-Smad or a Co-Smad.
- 1 Claim 42. (Withdrawn) A method of inhibiting TGF- β activity comprising the steps
2 of:
3 providing to a host in need of therapy a pharmaceutically effective amount of a
4 thioaptamer that specifically binds to and inhibits TGF- β activity.
- 1 Claim 43. (Withdrawn) The method of claim 42, wherein the thioaptamer is provided
2 to the host to ameliorate the effects of: fibrosis, scarring and adhesion during wound
3 healing; fibrotic diseases of the lung, liver and kidney; atherosclerosis, arteriosclerosis;
4 cancers including gliomas, colon cancer, prostate cancer, breast cancer, neurofibromas,
5 lung cancer; angiopathy, vasculopathy, nephropathy; systemic sclerosis; viral infections
6 accompanied by immune suppression (HIV, HCV); and immunological disorders and
7 deficiencies (auto-immune diseases).

- 1 Claim 44. (Withdrawn) A method of quantitating TGF- β levels in a sample
2 comprising the step of contacting a sample with a TGF- β -specific thioaptamer.
- 1 Claim 45. (Withdrawn) The method of claim 44, wherein the samples comprises a
2 physiological sample.
- 1 Claim 46. (Withdrawn) The method of claim 44, wherein the sample comprise a
2 blood, tissue, cells, supernatant, media.
- 1 Claim 47. (Withdrawn) The method of claim 44, wherein the TGF- β protein
2 comprises a human TGF- β .
- 1 Claim 48. (Withdrawn) The method of claim 44, wherein the TGF- β protein
2 comprises a TGF- β homodimer.
- 1 Claim 49. (Withdrawn) The method of claim 44, wherein the TGF- β protein
2 comprises a TGF- β 1, 2 or 3 heterodimer.
- 1 Claim 50. (Withdrawn) The method of claim 44, wherein the thioaptamer comprises
2 one or more thio-modifications as set forth in SEQ ID NOS.: 4-22.
- 1 Claim 51. (Withdrawn) The method of claim 44, wherein the thioaptamer further
2 comprises a detectable label.
- 1 Claim 52. (Withdrawn) The method of claim 44, wherein the thioaptamer further
2 comprises a detectable detectable selected from the group consisting of a colorimetric, a
3 fluorescent, a radioactive and an enzymatic agent.
- 1 Claim 53. (Withdrawn) A method of modulating TGF- β signaling comprising the
2 steps of:
3 administering to a host a TGF- β specific thioaptamer that modulates the activity through
4 the TGF- β receptor in a dosage effective to reduce activity of the TGF- β .

1 Claim 54. (Withdrawn) The method of claim 53, wherein the thioaptamer modulates
2 the activity through the TGF- β receptor by increasing activity.

1 Claim 55. (Withdrawn) The method of claim 53, wherein the thioaptamer modulates
2 the activity through the TGF- β receptor by decreasing activity.

1 Claim 56. (Withdrawn) The method of claim 53, wherein the thioaptamer is selected
2 from the group consisting of SEQ ID NOS.:4-22.

1 Claim 57. (Withdrawn) A method of treating a pathological condition due to
2 increased TGF- β activity comprising the steps of:
3 administering to a host an effective dosage of a thioaptamer that modulates TGF- β .

1 Claim 58. (Withdrawn) The method of claim 57, wherein the thioaptamer binds to
2 TGF- β , the TGF- β receptor, a TGF- β auxiliary protein, a TGF- β ligand binding trap
3 protein or a TGF- β Smad protein.

1 Claim 59. (Withdrawn) The method of claim 57, wherein the thioaptamer modulates
2 the activity through the TGF- β receptor by increasing activity.

1 Claim 60. (Withdrawn) The method of claim 57, wherein the thioaptamer modulates
2 the activity through the TGF- β receptor by decreasing activity.

1 Claim 61. (Withdrawn) The method of claim 57, wherein the thioaptamer is selected
2 from the group consisting of SEQ ID NOS.: 4-22.

1 Claim 62. (Withdrawn) The method of claim 57, wherein the pathological condition
2 comprises:
3 fibrosis, scarring and adhesion during wound healing; fibrotic diseases of the lung, liver
4 and kidney; atherosclerosis and arteriosclerosis; cancers such as gliomas, colon cancer,
5 prostate cancer, breast cancer, neurofibromas, lung cancer; angiopathy, vasculopathy,

- 6 nephropathy; systemic sclerosis; viral infections accompanied by immune suppression
7 (HIV, HCV); and immunological disorders and deficiencies (auto-immune diseases).

1 Claim 63. (Withdrawn) The method of claim 57, wherein the TGF- β specific
2 thioaptamer is encapsulated.

1 Claim 64. (Withdrawn) The method of claim 57, wherein the capsule is degradable
2 by an external stimulus to release the TGF- β specific thioaptamer.

1 Claim 65. (Withdrawn) The method of claim 57, wherein the external stimulus is
2 selected from the group consisting of UV light, acid, water, in vivo enzymes, ultrasound
3 and heat.

1 Claim 66. (Withdrawn) The method of claim 57, wherein the TGF- β specific
2 thioaptamer is bound to a binding molecule.

1 Claim 67. (Withdrawn) The method of claim 57, wherein the TGF- β specific
2 thioaptamer is bound to a binding molecule and further comprising the step of detaching
3 the binding molecule from the TGF- β specific thioaptamer.

1 Claim 68. (Withdrawn) A method of treating a pathological condition in which
2 increased TGF- β activity has been implicated comprising the steps of:
3 administering to a host a TGF- β specific thioaptamer in a pharmaceutically acceptable
4 carrier at a dosage effective to reduce TGF- β activity.

1 Claim 69. (Withdrawn) The method of claim 68, wherein the pharmaceutically
2 acceptable carrier is selected from the group consisting of a cream, gel, aerosol and
3 powder for topical application.

1 Claim 70. (Withdrawn) The method of claim 68, wherein the pharmaceutically
2 acceptable carrier is selected from the group consisting of a sterile solution for injection,
3 irrigation and inhalation.

- 1 Claim 71. (Withdrawn) The method of claim 68, wherein the pharmaceutically
2 acceptable carrier comprises a sterile dressing for topically covering a wound.
- 1 Claim 72. (Withdrawn) The method of claim 68, wherein the pharmaceutically
2 acceptable carrier is selected from the group consisting of a biopolymer and a polymer
3 for implanting within a wound.
- 1 Claim 73. (Withdrawn) The method of claim 68, further comprising the step of
2 administering a growth factor other than TGF- β .
- 1 Claim 74. (Withdrawn) The method of claim 68, wherein the TGF- β specific
2 thioaptamer is encapsulated.
- 1 Claim 75. (Withdrawn) A method of modulating TGF- β signaling comprising the
2 steps of:
3 administering to a host a TGF- β ligand binding trap specific thioaptamer that modulates
4 the activity through the TGF- β receptor in a dosage effective to reduce activity of the
5 TGF- β .
- 1 Claim 76. (Withdrawn) A method of modulating TGF- β signaling comprising the
2 steps of:
3 administering to a host a TGF- β auxiliary protein specific thioaptamer that modulates the
4 activity through the TGF- β receptor in a dosage effective to reduce activity of the TGF- β .
- 1 Claim 77. (Withdrawn) A method of modulating TGF- β signaling comprising the
2 steps of:
3 administering to a host a TGF- β Smad protein specific thioaptamer that modulates the
4 activity through the TGF- β receptor in a dosage effective to reduce activity of the TGF- β .

- 1 Claim 78. (Previously presented) A partially thio-modified aptamer that binds
- 2 specifically to TGF- β comprising a sequence and modifications that is at least 80%
- 3 complementary to SEQ ID NO: 62.